

# Breakthrough Reveals Potential FDA-Approved Parkinson's Treatment

### **Description**

Recent investigations have elucidated the mechanisms by which a cell surface protein known as Aplp1 facilitates the propagation of neurotoxic materials associated with Parkinson's disease from one neuron to another within the cerebral milieu.

Encouragingly, an FDA-sanctioned oncology medication that targets a distinct protein, <u>Lag3</u>—which exhibits a notable interaction with <u>Aplp1</u>—has been shown to inhibit this intercellular dissemination in experimental murine models, indicating that a viable therapeutic avenue may already be available.

In a <u>study published in the preceding year</u>, a multinational consortium of researchers articulates the intricate interplay between these two proteins, which is integral to the uptake of deleterious <u>alpha-synuclein</u> aggregates by neuronal cells.

Neuroscientist Xiaobo Mao from Johns Hopkins University remarked in June, "The elucidation of the Aplp1-Lag3 interaction provides a novel framework for comprehending how alpha-synuclein contributes to the pathogenesis of Parkinson's disease." He further emphasized that pharmacological targeting of this interaction could potentially decelerate the progression of both Parkinson's and other neurodegenerative disorders.

Globally, over <u>8.5 million individuals</u> are afflicted by Parkinson's disease, rendering it the second most prevalent neurodegenerative malady, following Alzheimer's. This progressive ailment, predominantly characterized by motor dysfunctions, is typically diagnosed post-manifestation of symptoms such as tremors, rigidity, and cognitive disturbances.

The degeneration of dopaminergic neurons in the <u>substantia nigra</u> underlies the symptomatic presentation of the disease, with the misfolding of alpha-synuclein implicated in the formation of toxic aggregates known as Lewy bodies.

Furthermore, prior murine studies <u>have demonstrated</u> that Lag3's binding to alpha-synuclein accelerates the spread of Parkinsonian pathology within neurons. While the ablation of Lag3 substantially mitigates this process, it does not entirely inhibit it, suggesting that additional proteins may also participate in mediating the absorption of misfolded alpha-synuclein within the neuronal framework.

The most recent experiments, employing genetically engineered mice deficient in Aplp1, Lag3, or both, revealed that, while Aplp1 and Lag3 can each independently facilitate the cellular uptake of detrimental alpha-synuclein, their simultaneous presence markedly amplifies this assimilation process. A striking reduction—up to 90 percent—of harmful alpha-synuclein ingress was observed in neurons lacking both proteins, underscoring the essential role of Aplp1.

The administration of the drug <u>nivolumab/relatlimab</u>, a therapeutic for melanoma that contains an antibody targeting Lag3, corroborated the inhibition of Aplp1-Lag3 interactions, effectively stymying the synthesis of pathological alpha-synuclein aggregates in neuronal cells.



At this juncture, the researchers intend to explore the efficacy of the Lag3 antibody in murine models of Parkinson's disease and Alzheimer's, the latter of which has also been highlighted as a potential avenue for targeted therapy according to emerging research.

This pivotal research has been disseminated in Nature Communications.

Note: An earlier iteration of this article was published in June 2024.

# **Vocabulary List:**

- 1. **Elucidated** /ɪˈluː.sɪ.deɪ.tɪd/ (verb): Made something clear; explained.
- 2. Intercellular /ˌɪn.tər'sel.jə.lər/ (adjective): Relating to or occurring between cells.
- 3. **Pathogenesis** / pæθ.oʊ'dʒɛn.ɪ.sɪs/ (noun): The development of a disease or the process by which a disease develops.
- 4. **Degeneration** /dɪˌdʒɛn.əˈreɪ.ʃən/ (noun): The process of losing functional or structural integrity.
- 5. **Absorption** /əbˈzɔːrp.ʃən/ (noun): The process by which one thing takes in or absorbs another.
- 6. **Therapeutic** /ˌθεrəˈpjuːtɪk/ (adjective): Relating to the treatment of a disease or a medical condition.

# **Comprehension Questions**

#### **Multiple Choice**

1. What is the cell surface protein that facilitates the propagation of neurotoxic materials associated with Parkinson's disease?

Option: Aplp1 Option: Lag3

Option: Alpha-synuclein

Option: Nivolumab/relatlimab

2. Which protein has been shown to inhibit intercellular dissemination in experimental murine models related to Parkinson's disease?

Option: Aplp1 Option: Lag3

Option: Alpha-synuclein
Option: Nivolumab/relatlimab



3. What is the degeneration of dopaminergic neurons in the substantia nigra implicated in?

Option: Lewy bodies formation
Option: Alpha-synuclein misfolding

Option: Alzheimer's disease
Option: Parkinsonian pathology

4. Which drug contains an antibody targeting Lag3 and inhibits Aplp1-Lag3 interactions?

Option: Aplp1 Option: Lag3

Option: Alpha-synuclein

Option: Nivolumab/relatlimab

5. What did experiments on genetically engineered mice deficient in Aplp1 and Lag3 reveal?

Option: Ablation of Lag3 inhibits assimilation process

Option: Simultaneous presence of ApIp1 and Lag3 reduces ingress by 90%

Option: Lack of Aplp1 reduces intercellular dissemination

Option: Aplp1 and Lag3 independently inhibit alpha-synuclein absorption

6. What does the research intend to explore the efficacy of in murine models of Parkinson's disease and Alzheimer's?

Option: Aplp1-Lag3 interactions

Option: Alpha-synuclein aggregates

Option: Lag3 antibody

Option: Nivolumab/relatlimab activity

#### **True-False**

- 7. Lag3 is a cell surface protein implicated in the propagation of neurotoxic materials associated with Parkinson's disease.
- 8. Alpha-synuclein misfolding is not involved in the formation of Lewy bodies.
- 9. Administering nivolumab/relatlimab has no impact on the synthesis of pathological alpha-synuclein aggregates in neuronal cells.
- 10. Alpha-synuclein contributes to the pathogenesis of Alzheimer's disease as well.
- 11. The recent research on Parkinson's disease was disseminated in Journal of Neuroscience.



**Gap-Fill** 

12. The research intends to explore targeted therapy for Huntington's disease.

13. According to the content, over million individuals globally are afflicted by					
Parkinson's disease.					
15. The administration of nivolumab/relatlimab, a therapeutic for melanoma, effectively stymies the					
synthesis of in neuronal cells.					
16. According to the content, the degeneration of neurons in the substantia nigra					
underlies the symptomatic presentation of Parkinson's disease.					
17. The most recent experiments showed that the simultaneous presence of Aplp1 and Lag3 markedly					
amplifies the assimilation process of detrimental					
18. The multinational consortium of researchers articulated the intricate interplay between Aplp1 and Lag3,					
which is integral to the uptake of deleterious by neuronal cells.					

# **Answer**

**Multiple Choice:** 1. Aplp1 2. Lag3 3. Lewy bodies formation 4. Nivolumab/relatlimab 5. Simultaneous presence of Aplp1 and Lag3 reduces ingress by 90% 6. Lag3 antibody

True-False: 7. False 8. False 9. False 10. False 11. False 12. False

Gap-Fill: 13. 8.5 15. pathological alpha-synuclein aggregates 16. dopaminergic 17. alpha-synuclein

18. alpha-synuclein aggregates

# Vocabulary quizzes

### Multiple Choice ( Select the Correct answer for each question. )

1. What term is used to describe something that has been explained in a clear and detailed manner?

Option: Absorption



Option: Degeneration Option: Elucidated Option: Therapeutic

2. Which term refers to the origin and development of a disease?

Option: Mitigating Option: Pathogenesis Option: Intercellular Option: Taxonomic

3. Which term means inspiring fear or respect through being impressively large powerful intense or capable?

Option: Formidable Option: Ecological Option: Phenotypic Option: Modulate

4. Which term relates to the healing of a disease or the treatment of a disorder? NEWS.CO

Option: Intrinsic Option: Therapeutic Option: Delineate Option: Antisocial

5. What is the term used to describe a statistical analysis that combines the results of multiple scientific studies?

Option: Meta-analysis Option: Prophylaxis Option: Mitigating Option: Inherent

6. Which term means to support strengthen or reinforce something?

Option: Obscured Option: Bolster Option: Emblematic Option: Augmented

7. What term describes a pattern of behavior that is harmful or disruptive to others in society?

Option: Exquisite Option: Antisocial Option: Artistry Option: Mortality

8. Which term means to regulate adjust or control something?



Option: Discern Option: Modulate Option: Acquity Option: Vital

9. What term is used to describe something that is not clear or hidden from view?

Option: Inherent
Option: Obscured
Option: Delineate
Option: Degeneration

10. Which term means to make something greater by adding to it?

Option: Augmented Option: Acquity Option: Vital Option: Mortality

# Gap-Fill (Fill in the blanks with the correct word from the vocabulary list.)

11	is the sharpness or keenness of thought vision or hearing.				
12	refers to the deterior	ation or weakening o	of something es	pecially over time.	
13. Proper nutrition is	for	r maintaining good h	ealth.		
14. Her	talent for music	became evident at a	very young age	2.	
15. The scientist studied the		impact of defore	estation on local	l wildlife.	
16. The government introduce	ed new policies to rec	luce infant		rates.	
17. The study focused on the		characteristics	displayed by the	e new species.	
18. The artist was able to		the intricate details	of the landsca	pe in his painting.	
19. The hiker was saved by th	e timely administrati	on of	afte	r being bitten by a	
snake.					
20. Regular hand washing is a	simple form of		against the spr	read of infectious	



diseases.

### Matching Sentences (Match each definition to the correct word from the vocabulary list.)

- 21. The professor the complex theory to the students in a way that was easy to understand.
- 22. Communication between cells occurs through signaling molecules.
- 23. The bald eagle is of strength and freedom in the United States.
- 24. The researchers conducted a of existing studies to draw comprehensive conclusions.
- 25. Her talent for storytelling was and had been evident since she was a child.
- 26. The ability to subtle differences in color is essential for a painter.
- 27. The chef's culinary was evident in the beautifully presented dishes.
- 28. Planting more trees is a factor in reducing air pollution.
- 29. The jewelry was crafted with detail and precision.
- 30. The scientist carefully outlined the experimental before conducting the research.

### Answer

**Multiple Choice:** 1. Elucidated 2. Pathogenesis 3. Formidable 4. Therapeutic 5. Meta-analysis 6. Bolster 7. Antisocial 8. Modulate 9. Obscured 10. Augmented

**Gap-Fill:** 11. Acquity 12. Degeneration 13. Vital 14. Intrinsic 15. Ecological 16. Mortality 17. Phenotypic 18. Delineate 19. Antivenom 20. Prophylaxis

**Matching sentence:** 1. Elucidated 2. Intercellular 3. Emblematic 4. Meta-analysis 5. Inherent 6. Discern 7. Artistry 8. Mitigating 9. Exquisite 10. Methodology

#### **CATEGORY**

1. Health - LEVEL6

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